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EXAMINER	
ARNOLD, ERNST V	

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1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/557,192	DU PLESSIS, TJAART ANDRIES	
	Examiner	Art Unit	
	ERNST V. ARNOLD	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *1-20 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-37 and 39* is/are rejected.

7)☒ Claim(s) *39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/28/09; 11/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group II, claims 21-37 and 39, in the reply filed on 5/27/09 is acknowledged. Claims 1-20 and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim.

Claims 40 and 41 have been cancelled. Claims 21-37 and 39 are presented for examination on the merits. The Examiner is examining the kit claims as they read on a composition.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Foreign language reference DE 2620773 has only been considered to the extent that the international search report categorizes it as an "A" reference.

Claim Objections

Claim 39 is objected to because of the following informalities: claim 39 is dependent on a withdrawn claim. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 39 is rejected under 35 U.S.C. 102(b) as being anticipated by Gertzman et al. (US 6437018).

Gertman et al. disclose a sterile composition comprising osteoinductive bone powder (claim 1) with irradiated sodium hyaluronate (claims 8 and 12) using gamma radiation (column 15, lines 43-53). Flowable gels and malleable puttys are disclosed (see Examples I-VI). Thus instant claim 39 is anticipated.

With respect to the USC 102 rejection above, please note that in product-by-process claims, "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 102 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). In addition, please note that the Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether Applicants' osteoinductive agent biopolymer differs and, if so, to what extent, from that of the discussed reference.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21, 22, 25, 26, 28, 35, 36, 37 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Phillips et al. US 20030027883.

Phillips et al., which is Applicant's own work, discloses in claims 1-6:

> 1. A process for modifying a naturally occurring biocompatible biopolymer, said process comprising subjecting said biopolymer, in the solid, or dry state, to a source of ionizing radiation in the presence of a mediating gas and annealing the resulting product in the absence of oxygen at a temperature of about 40 to 120° C., and thereafter removing any residual mediating gas.
>
> 2. A process according to claim 1 wherein the source of the ionizing radiation is a γ-ray emitting radioactive isotope, X-rays or high energy radiation generated by an electron accelerator.
>
> 3. A process according to claim 2 wherein the dose of ionizing radiation to which the biopolymer is subjected to is from about 1 to 50 kGy.
>
> 4. A process according to claim 2 wherein the radioactive isotope is ^{60}Co.
>
> 5. A process according to claim 2 wherein the radiation is generated by an electron generator of 250 KeV to 10 MeV capacity.
>
> 6. A process according to claim 1 wherein the mediating gas is an unsubstituted alkenic or alkynic gas, and is ethylene, propylene or acetylene.

And in claims 9-11:

9. A process according to claim 1 wherein annealing is effected in the presence of the mediating gas, an inert gas or in vacuo.

10. A process according to claim 9 wherein the inert gas is nitrogen or helium.

11. A process according to claim 1 wherein removal of any residual mediating gas is effected by aerating the system and optionally, additionally applying vacuum.

Phillips et al. teach hyaluronan, collagen and demineralized bone as the biopolymer (claims 16, 21 and 24). Phillips et al. disclose in claims 32-36:

32. A process for modifying a tissue of animal origin, said process comprising subjecting said tissue sample or a component thereof in the solid, or dry state, to a source of ionizing radiation in the presence of a mediating gas and annealing the resulting product in the absence of oxygen at a temperature of about 40 to 120° C., and thereafter removing any residual mediating gas.

33. A process according to claim 32 wherein tissue is bone ray emitting radioactive isotope, X-rays or high energy radiation generated by an electron accelerator.

34. A process according to claim 33 wherein the bone is whole bone or demineralized bone.

35. A process according to claim 34 wherein the tissue is soft tissue.

36. A modified biopolymer produced by the process as claimed in claim 1.

Phillips et al. disclose triple packaging demineralized bone which can be used to prepare and dispense the demineralllized bone which is an osteoinductive agent [0147]. Thus, the subject matter of instant claims 21, 22, 25, 26, 28, 35, 36, 37, and 39 is anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 21-37 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips et al. (US 6610810) in view of Saito et al. (EP 0739638) and Benedict et al. (US 6679918).

Applicant claims a kit for preparing and dispensing an osteoinductive agent including a modified naturally occurring biocompatible biopolymer which was subjected, in the solid, or dry state, to a source of ionising radiation in the presence of a mediating gas and annealed in the absence of oxygen at a temperature of from 40°C to 120°C to render the product in a dry particulate form, the product being disposed in a hermetically sealed container containing oxygen-free gas.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Phillips et al., which is Applicant's own work, teach how to modify naturally occurring biocompatible biopolymers such as collagen, hyaluronan, and demineralized bone in the presence of a mediating gas such as acetylene, ethylene or propylene with ionizing radiation from about 1 to 50 kGy (Abstract; column 3, lines 17-50; column 21, lines 40-63; and claims 1-53). The product is annealed in the absence of oxygen in the presence of an inert gas such as nitrogen or helium at a temperature of about 40 to 120 C (column 4, lines 18-30; and claim 1). Phillips et al. teach in column 3, lines 50-60:

> In carrying out the process of the invention for producing the new materials from the starting biopolymers, it is preferred that the biopolymer be in its original solid state, i.e., dry, in an atmosphere comprising a mediating agent, preferably a low molecular weight unsaturated alkenic or alkynic gas such as ethylene, propylene or acetylene, preferably acetylene. Before introducing the mediating gas to the reaction site, the site must be flushed to remove therefrom any active, oxygen containing atmosphere. All the mediating gas is removed after completion of the process and therefore, the resulting new materials do not contain any of the mediating gas.

Phillips et al. teach that demineralized bone can be endowed with up to four times greater bone healing characteristics (column 26, lines 40-59; column 28, lines 5-18 and column 29, lines 13-21). Phillips et al. teach triple packaging and terminal sterilization (column 27, lines 22-24). In the absence of evidence to the contrary, the packaging is hermetically sealed.

Saito et al. teach the concept of sterilizing pre-filled syringes (Abstract; column 5, lines 20-28 and claims 1-5). An aseptic prefilled syringe kit concept is taught (column 5, lines 29-44). Saito et al. teach using an autoclave for sterilization in claim 4 but do not limit claim 1 to the type of sterilization process. In Figures 1-3 it can be seen that the syringe is the primary container and the package is the sealed secondary container.

Benedict et al. teach sterilization of osteogenic compositions that contain collagen, *water*, and demineralized bone material, which would include demineralized bone matrix, with ethylene oxide (column 8, lines 14-23 and claims 1, 9, 10, and 14) and by gamma radiation (claim 11). Benedict et al. teach kits of the material (column 8, lines 24-36 and claim 16). Thus, Benedict et al. establish the concept of sterilizing osteogenic kit compositions.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. The difference between the instant application and Phillips et al. is that Phillips et al. do not expressly teach subjecting the biopolymers separately to the ionizing radiation and then mixing; mixing the biopolymers first and then subjecting them to the ionizing radiation; an outlet opening diameter of larger than 0.6 mm on the syringe container; a second primary container containing a liquid which is pyrogen free water; disposing the secondary container inside a third hermetically sealed container which is filled with oxygen free gas; the secondary and tertiary containers are vacuum formed from a radiation stable, gas impermeable material.

2. The difference between the instant application and Phillips et al. is that Phillips et al. do not expressly teach a primary container in the form of syringe type container. This deficiency in Phillips et al. is cured by the teachings of Saito et al. and Benedict et al.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to subjecting the biopolymers separately to the ionizing radiation and then mixing; mixing the biopolymers first and then subjecting them to the ionizing radiation; an outlet opening diameter of larger than 0.6 mm on the syringe container; a second primary container containing a liquid which is pyrogen free water; disposing the secondary container inside a third hermetically sealed container which is filled with oxygen free gas; the secondary and tertiary containers are vacuum formed from a radiation stable, gas impermeable material, a terminal radiation process is used on the composition of Phillips et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because these are merely either selection of process steps or design choices. Selecting mixtures of biopolymers is merely a design choice when all the biopolymers are taught by the art. From MPEP 2144.04: In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA

1930) (Selection of any order of mixing ingredients is prima facie obvious.). The expected result is sterilized biopolymers in sterilized containers. It does not matter if there is one or one thousand hermetically sealed containers. The concept is already public knowledge. In the absence of evidence to the contrary, the water is pyrogen free.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make a kit of the composition of Phillips et al. with a primary container in the form of syringe type container, as suggested by Saito et al. and Benedict et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because the art teaches a making kits of osteogenic compositions as taught by Benedict et al. and Saito et al. provide syringes for dispensing the osteogenic composition.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 21-37 and 39 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 6-10, 14, 16, 20-22, 25-28, 36, 37, 43, and 48-50 of U.S. Patent No. (US 6610810) in view of Saito et al. (EP 0739638) and Benedict et al. (US 6679918). The rejection is set forth above and that rejection is hereby incorporated by reference. One of ordinary skill in the art would recognize the obvious variation of the instant subject matter over the patent in view of the cited references.

2. Claims 21-37 and 39 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 6-9, 12, 18, 23, 29-32 and 34 of U.S. Patent No. (US 6610810) in view of Saito et al. (EP 0739638) and Benedict et al. (US 6679918). The references of Saito et al. and Benedict et al. are discussed in detail above and those discussions are hereby incorporated by reference.

US 6841644 discloses in claims 1-3:

> 1. A modified naturally occurring biocompatible biopolymer selected from the group consisting of polysaccharides of microorganism, plant or animal origin, a protein of animal connective tissue origin, a protein of other animal tissue origin, a combination of at least one of said polysaccharides and at least one other protein of plant origin and demineralized bone, and which is produced by a process comprising subjecting said biopolymer in the solid or dry state, to a source of ionizing radiation in the presence of a mediating gas which is an unsubstituted alkynic gas and annealing the resulting product in the absence of oxygen at a temperature of about 40° to 120° C., and thereafter removing any residual mediating gas.
>
> 2. A modified biopolymer according to claim 1 wherein in the process, the source of the ionizing radiation is a γ ray emitting radioactive isotope, X-rays or high energy radiation generated by an electron accelerator.
>
> 3. A modified biopolymer according to claim 2 wherein in the process, the dose of ionizing radiation to which the biopolymer is subjected to is from about 1 to 50 kGy.

US 6841644 does not expressly teach a kit with a syringe in a container. However, Saito et al. and Benedict et al. teach sterilizing pre-filled syringes. It is merely a matter of placing the biopolymer in the syringe into a hermetically sealed package for sterilization and sterilization of osteogenic compositions is known in the art. One of ordinary skill in the art would have recognized the obvious variation of the instant subject matter over the patent in view of the cited references.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ernst V Arnold/
Examiner, Art Unit 1616